

1) Protocol Title

Include the full protocol title as listed on the application form.

**Acceptance and Commitment Therapy vs. Supportive Psychotherapy with
Cystic Fibrosis Patients**

2) IRB Review History

If you have submitted this protocol for review by an external IRB, provide the previous study identification number and provide details of the review including the IRB name, date of review, and IRB contact information.

Not applicable.

3) Objectives

Describe the purpose, specific aims, or objectives.

State the hypotheses to be tested.

The objective of the study is to assess the utility of “Acceptance and Commitment Therapy” (ACT) in which subjects learn new ways to manage uncomfortable experiences and feelings and to engage in positive behaviors, over “Supportive Psychotherapy” in which subjects talk about their experiences to date in a cohort of adult Cystic Fibrosis patients. The hypothesis is that six telehealth/webcam sessions of ACT will lead to an improvement in medication and visit compliance, as well as an overall improved sense of well-being and coping skills, particularly as compared with 6 telehealth/webcam sessions of supportive psychotherapy.

4) Background

Describe the relevant prior experience and gaps in current knowledge.

Describe any relevant preliminary data.

Provide the scientific or scholarly background for, rationale for, and significance of the research based on the existing literature and how the research will add to existing knowledge.

Rationale.

Cystic fibrosis is an autosomal recessive genetic disease with an average lifespan of about 37 years of age. These patients are generally diagnosed at birth and have to keep up with a tremendous amount of daily therapies including airway clearance and taking pancreatic enzymes before every meal. Not surprisingly, patients with cystic fibrosis often struggle with depression issues, especially as they begin to enter adolescence as well as beyond. (1,2) Depression has been

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associated with lower lung function, the biggest contributor to morbidity and mortality in the cystic fibrosis population. (3)

Dr. O'Hayer completed a three-year study evaluating the feasibility and effectiveness of ACT with CF (Protocol 1602004239) in treating anxiety and depressive symptoms in 30 patients with CF. The study showed that ACT with CF was associated with 1) decreased anxiety from baseline to completion (6 weeks), 2) decreased depression from baseline to completion and at 3 months post-treatment, 3) decreased cognitive fusion from baseline to completion and at 3 months post treatment, 4) improved FEV₁/FVC ratio, and 5) improved medication adherence and reduced problematic behaviors to cope with anxiety/avoidance. All participants reported positive and favorable "user" experience with ACT treatment modality, expressing a strong desire to continue ACT sessions.

By the end of the study, all participants reported reduction in anxiety and depressive symptoms after receiving six 50-minute ACT treatment sessions. This feasibility study also demonstrated that ACT treatment was associated with durable reduction of cognitive fusion (rigid attachment to one's thoughts as Truth) and lung function improvement (measured by FEV₁/FVC ratio).

Significantly, the study provided patients with a choice of in-person or telehealth intervention delivery. Of 30 participants, 24 selected telehealth, and this modality was found to be as effective as in-person ACT with CF. Also important, ACT treatment sessions were delivered by ten MA-level graduate students trained for one day in the ACT with CF protocol. All ten students were trained and supervised by Dr. O'Hayer.

These pilot data generated several questions:

- Would a randomized controlled trial produce results as strong as the pilot study?
- Does ACT improve medication adherence?
- Does ACT help sicker people (e.g., CF patients awaiting lung transplantation)?
- Does ACT work better than just talking with someone: Will ACT be more effective than treatment as usual (supportive psychotherapy)?
- Why did ACT improve lung function?
- Was it because of improved health behaviors: medications, exercise, pulmonary rehab?
- Did reduced anxiety among patients cause less medication avoidance?
- Were patients less depressed and therefore more active, encouraging positive lung effects?

Given this need within our patient population, we would like to undertake a study of the use of a six-week intervention to improve mental health. There is no data published in the

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literature to help guide which intervention would work well in the cystic fibrosis population, and we would like to work on this study to help fill in this gap in knowledge.

References:

1. Goldbeck L, Besier T, Hinz A, et al. Prevalence of symptoms of anxiety and depression in German patients with cystic fibrosis. *Chest* 2010;138:929–36.
2. Quon BS, Aitken ML. Cystic fibrosis: what to expect now in the early adult years. *Pediatric Respir Rev* 2012;13: 206–14.
3. Riekert KA, Bartlett SJ, Boyle MP, et al. The association between depression, lung function, and health-related quality of life among adults with cystic fibrosis. *Chest* 2007;132:231–7.
4. O’Hayer CV, Bennett, DS, Wolfe W, Juarascio A, & Marino E. (2016) ACT with CF -Reducing anxiety & depression among individuals with cystic fibrosis through Acceptance and Commitment Therapy: A treatment manual. Philadelphia, PA: Drexel University Department of Psychiatry.
5. Harris, R. (2008). *The happiness trap: How to stop struggling and start living*. Boston, MA, US: Trumpeter Books.
6. Harris, R. (2009). *ACT Made Simple: An Easy-To-Read Primer on Acceptance and Commitment Therapy*. Oakland, CA: New Harbinger.
7. Luoma, J. B., Hayes, S. C., & Walser, R. D. (2007). *Learning ACT: An acceptance and commitment therapy skills-training manual for therapists*. Oakland, CA, US: New Harbinger Publications.
8. Hayes, L. L., & Ciarrochi, J. (2015). *The thriving adolescent: Using Acceptance and Commitment Therapy and positive psychology to help teens manage emotions, achieve goals, and build connection*. New Harbinger Publications.
9. O’Hayer, C.V., Nurse, C.N., Aikens, R., O’Loughlin, C.M., Bennett, D. S.Hem Lee, M. A., Hendry M. & Stephen, M.J.. (2018). ACT With CF: Promising Conclusions Of A Telehealth Pilot Study Of Acceptance And Commitment Therapy For Anxiety And Depression. The North American Cystic Fibrosis Conference (NACFC).

5) Inclusion and Exclusion Criteria

Describe how individuals will be screened for eligibility.

All patients who attend the cystic fibrosis clinic at our recruitment sites (currently Drexel University, Children’s Hospital of Philadelphia, University of Pennsylvania Medical Center, St. Christopher’s Hospital for Children, Duke University Medical Center, Augusta University and the University of Pittsburg) will be eligible for inclusion in the study. Chelsi Nurse, a Research Assistant of Dr. O’Hayer’s will visit the local clinics (UPenn, St. Chris, Drexel, CHOP) to do the consent process. At satellite sites, patients will be consented by our site representative. We will screen all CF patients for depression and anxiety, and solicit their interest participating in the study. There are no subjects under the age of 18 in

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either of the clinics, and none will be accepted from other sites. Prisoners will be excluded inclusion into the study given potential time constraints given the need for six counseling sessions. We will not be recruiting adults unable to consent.

Individuals will be screened for eligibility via PHQ-9 > 4 or GAD-7 > 4 (the cutoff of 5 is typically used for both of these measures to suggest mild symptoms of depression or anxiety, respectively); and the BDI-II > 13 or BAI > 9 (the cutoff of 14 is typically used for the BDI to suggest mild symptoms of depression, and the cutoff of 10 is typically used for the BAI to suggest mild symptoms of anxiety). We are using two measures of anxiety and two measures of depression, to maximize the likelihood that patients experiencing clinically relevant symptoms are detected and referred to this study.

Describe the criteria that define who will be included or excluded in your final study sample.

Main Inclusion Criteria

- Men and women aged 18 and above.
- Able to read/understand English.
- Diagnosis of cystic fibrosis.
- PHQ-9 score > 4 or GAD-7 score > 4.

Main Exclusion Criteria

- History of suicidal attempts or acute suicidal ideation on clinical assessment.
- Presence of psychotic disorder or symptoms.
- Pregnant women.
- Presence of psychiatric disorders that interfere with the participation of the study, judged by the study or treating clinician. Presence of other medical conditions that interfere with participation in the study, judged by the study or treating clinician.

Indicate specifically whether you will include each of the following special populations, one or more boxes must be checked (You may not include members of these populations as subjects in your research unless you indicate this in your inclusion criteria.)

- ☐ Adults unable to consent
- ☐ Individuals who are not yet adults (infants, children, teenagers)
- ☐ Pregnant women
- ☐ Prisoners
- ☒ Not Applicable

6) Study-Wide Recruitment Methods

If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods.

Describe when, where, and how potential subjects will be recruited.

Describe the methods that will be used to identify potential subjects.

Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

This is a multi-center study, in which subjects from Drexel, UPenn, CHOP and St. Christopher's Hospital will be recruited in the cystic fibrosis clinic during their normal follow up visits. Research assistant Chelsi Nurse will be obtaining consent at Children's Hospital of Philadelphia, University of Pennsylvania Medical Center, Adult Cystic Fibrosis Center at Drexel Pulmonary Medicine, and St. Christopher's Hospital for Children. All CF patients will be approached to assess interest. Referrals may be accepted from Cystic Fibrosis centers not participating in this study, and in this case Chelsi Nurse will travel to the local CF clinic and consent each of these subjects in person. Subjects will be recruited from remote sites (Duke Univ Med Center, Augusta Univ, U Pittsburg) by our on-site representatives Chris Drescher (Augusta University), Patrick Smith and current research assistants (Duke University) and the current Cystic Fibrosis social worker (University of Pittsburg).

Potential subjects will be recruited at the following sites over a 3-year trial period:

- Children's Hospital of Philadelphia
- University of Pennsylvania Medical Center
- Adult Cystic Fibrosis Center at Drexel Pulmonary Medicine
- St. Christopher's Hospital for Children
- Duke University Medical Center
- Augusta University
- University of Pittsburg

7) Study Timelines

Describe:

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- *The duration of an individual subject's participation in the study.*

Subjects will actively participate in the study for a total of approximately six months. This will include enrollment, six weeks of counseling and then a three month follow up when they will complete the exit questionnaire. We will then continue to follow their clinical course for another nine months, including any exacerbations, missed follow up visit, and decline in FEV1. We complete follow up and data collection with each patient within one year. We will then complete the primary analysis, to complete by 06/30/2022.

We expect that participants will be attend 6 weeks of telehealth/webcam therapy (once a week) and complete questionnaires 3 months after this therapy.

- *The duration anticipated to enroll all study subjects.*
The duration anticipated to enroll all study subjects is 3 years.
- *The estimated date for the investigators to complete this study (complete primary analyses.*

The estimated date for completion of primary analyses is 6 months after the end of study enrollment. Data will be stored for seven years after study completion, as per institutional policies and procedures.

- *If using medical or electronic records indicate the time span of the data to be collected; (DATE OF RECORDS FROM ____; DATE OF RECORDS ENDING ____.)*

We will examine medical/electronic records for each individual that covers the 3-month period following the subject's study intake, 3 months prior to subject's study intake, and 3 months post study.

Study Endpoints

Describe the primary and secondary study endpoints, or goals the investigator intends to achieve, prove or disprove. Primary endpoints measure outcomes that will answer the primary, or most important, questions being asked by the research protocol.

The primary study endpoints will be an improvement in the primary questionnaires given to the patient, which will be given to the patients at the time of enrollment, at the completion of treatment and then three months after the six intervention sessions are completed. Secondary endpoints will be any changes in lung function, specifically changes in patients FEV1, along with compliance with appointments, and number of exacerbations per year. These outcomes will be compared for the year prior to counseling with the year after counseling. For those subjects not at Drexel, the local site representative will input the data through a link that puts data into Drexel Redcap.

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Primary Endpoints:

- Changes of GAD from baseline, to treatment session completion, and 3 months follow-up
- Changes of PHQ-9 from baseline, to treatment session completion, and 3 months follow-up
- Change in Beck Anxiety Inventory from baseline, to treatment session completion, and 3 months follow-up
- Change in Beck Depression Inventory from baseline, to treatment session completion, and 3 months follow-up

Secondary Endpoints:

- Change in FEV1/FVC ratio
- Change in cognitive fusion (rigid attachment to one's thoughts as Truth) measures
- Change in acceptance measures
- Change in medication adherence
- Rehospitalization and unscheduled office visits secondary to CF exacerbations
- Scheduled CF clinic visits kept
- Change in Body Mass Index (BMI)
- Patient rated outcomes measures (PRO) including quality of care questionnaires

Describe any primary or secondary safety endpoints

N/A.

Participants will be asked to complete a series of brief questionnaires at the time of their intake, after 6 appointments and 3-months after their sixth appointment.

8) Procedures or Methods Involved

Describe and explain the study design.

Provide a description of all research procedures being performed and when they are performed, including procedures being performed to monitor subjects for safety or minimize risks.

Describe:

- *Procedures performed to lessen the probability or magnitude of risks.*
- *All drugs and devices used in the research and the purpose of their use, and their regulatory approval status.*
- *What data will be collected including long-term follow-up.*
- *Indicate below the source records that will be used to collect data about subjects. (Attach all surveys, scripts, and data collection forms.)*

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Patients will be consented in the adult cystic fibrosis clinic at Drexel University, Children's Hospital of Philadelphia, University of Pennsylvania Medical Center, St. Christopher's Hospital for Children, Duke University Medical Center, Augusta University and the University of Pittsburgh. For Philadelphia sites (CHOP, Drexel, UPenn, St. Chris), Chelsi Nurse will consent patients to treatment. If at remote sites (Duke Univ Med Center, Augusta Univ, U Pittsburgh) by our local site appointed representatives will consent patients to the study. All CF patients will be approached to assess interest.

If patients are willing to be in the study, they will be given a packet of screening questionnaires (addendum #1). These questionnaires will ask patients: 1) how often you experience different thoughts and feelings, including some related to having cystic fibrosis; 2) how often you take your cystic fibrosis medications; 3) your coping style, including how long you persist in thinking about something that has happened to you; The subject will complete each questionnaire again after 6 appointments (i.e., about 6 weeks later), and again about 3-months after their sixth appointment.

Finally, we hope to learn whether these therapies affect how often subjects take their cystic fibrosis medications, and how this affects their health and wellbeing. To study this, we will review the number of appointments that are missed six months before enrolling in the program, and six months after completing therapy. We will also review their pulmonary function tests, whether subjects go to the hospital or see their doctor for any extra visits, and the presence of any ongoing symptoms of depression or anxiety. All data will be taken from Allscripts, the Drexel outpatient medical chart. Data will be taken only from the departments of the pi and co-pi's. At UPenn, the social worker at the site will input data into Drexel Redcap through a link sent to them.

Participants will complete 6 sessions of our ACT with CF manualized intervention. Please see attached manual.

Participants will be asked to complete a series of brief questionnaires at the time of consent. If desired, they can take these homes to complete and mail back. These questionnaires will ask participants about: 1) how often they experience different thoughts and feelings, including some related to having cystic fibrosis; 2) how often they take their cystic fibrosis medications; 3) their coping style, including how long they persist in thinking about something that has happened to you (see Addendum 1 for full list of questionnaires).

Participants will complete each questionnaire again after 6 appointments (i.e., about 6 weeks later), and again about 3-months after their sixth appointment.

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These questionnaires take about 45 minutes to complete. Participants will also be asked to complete 6 'Zoom' therapy sessions (using a webcam in their own home or on their own tablet/smartphone and HIPAA-compliant Zoom webcam service) of either "Acceptance and Commitment Therapy", in which participants will learn new ways to manage uncomfortable experiences and feelings (e.g., depression, anxiety) and to engage in positive behaviors, or to "Supportive Psychotherapy", in which participants will talk about their experiences to date. The type of therapy that participants get will be chosen by chance, like flipping a coin. Neither subject nor the study doctor will choose what treatment the participant will get.

Participants will have an equal chance of being given each therapy. Audio and video recordings will be taken during each 'Zoom' therapy session. Recordings will be kept on password encrypted USB drives and stored in a locked office only accessible to the principal investigator and adherence coder.

Finally, we hope to learn whether these therapies affect how often participants take their cystic fibrosis medications, and how this affects their health and wellbeing. To study this, we will review information from medical charts such as the number of appointments that kept, the number of appointments missed, pulmonary function tests, number of hospital or doctor visits, and the presence of any symptoms of depression or anxiety.

Measures administered are as follows:

Page 1-2: Demographics

Page 3-6: CFMHQ: CF Mental Health and Wellness Self-Report Measure. (O'Hayer et al., 2019.)

Page 7-8: BDI-II: Beck Depression Inventory-II. (1996 Aaron T. Beck. Pearson. PsychCorp. Product #0154018392)

Page 9: BAI: The Beck Anxiety Index. Pearson. (Product #0154018422)

Page 10-13: CFQ-R: Cystic Fibrosis Questionnaire-Revised. (2000, Quittner, Modi, Watrous and Messer. Revised 2002. CFQ-R Teen/Adult.)

Page 14: Medical Coping Modes Questionnaire. (Feifel H, Strack S, Nagy T. 1987. Coping strategies and associated features of medically ill patients. *Psychosomatic Medicine* ;49:616-625.)

Page 15: CFS: Coping Flexibility Scale. (Kato, T. 2012. Development of the Coping Flexibility Scale: Evidence for the coping flexibility hypothesis. *Journal of Counseling Psychology*, 59(2), 262-273.)

Page 16: My CF Treatments: Treatment Adherence Questionnaire-CF. (Quittner, A. L., Modi, A. C., Lemanek, K. L., Ievers-Landis, C. E., & Rapoff, M. A. 2008. Evidence-based assessment of adherence to medical treatments in pediatric psychology. *Journal of pediatric psychology*, 33(9), 916-938.)

Page 17-18: ACT Demographics

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Page 19: CFQ13: Cognitive Fusion Questionnaire. (CFQ-13; Gillanders et al., 2014)

Page 20: Short Grit Scale (Duckworth, A.L. & Quinn, P.D. 2009. Development and validation of the Short Grit Scale (GritS). *Journal of Personality Assessment*, 91, 166-174.)

Page 21: AAQ-II: Acceptance and Action Questionnaire. (Bond et al.)

Page 22-23: Styles of Coping Word-Pairs. (Lynch, T.R. 2015.)

9) Data and Specimen Banking

If data or specimens will be banked for future use, describe where the specimens will be stored, how long they will be stored, how the specimens will be accessed, and who will have access to the specimens.

List the data to be stored or associated with each specimen.

Describe the procedures to release data or specimens, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

Data will be stored in Redcap, a secure HIPAA compliant Drexel database for a total of seven years after study completion.

10) Data Management

Describe the data analysis plan, including any statistical procedures.

We will attempt to recruit two hundred and ten subjects in total. We will analyze the data with each subject serving as their own control, with the first packet of questionnaires prior to counseling being compared with the questionnaires immediately after counseling and then three months after counseling. We will use a standard data analysis using a two-tailed t-test to see if there are significant differences between their responses in the first set of questionnaires before counseling to the second set after counseling.

We will also analyze data for the ACT condition compared with data from the Supportive Psychotherapy condition, using a standard data analysis using a two-tailed test, and also using multiple regression

Data will be collected on printed sheets, and then be manually entered into Drexel Redcap. Only the pi, co-pi's and research coordinator will have access to the Redcap database. Once the primary data is placed into Redcap, the paper forms will be destroyed. Data will not be sent outside of Drexel University. Data will be password-protected and stored on RedCap. Paper forms will also be stored in a locked cabinet inside a locked office, and then destroyed once data are entered into RedCap. The one data key sheet that includes patient name and associated subject number will also be stored in a locked cabinet inside a locked office and destroyed at the end of the research.

Describe how data will be handled study-wide:

- Physical data will be stored in locked file cabinets only accessible by researchers. Electrical data will be store on password protected computers in the locked researcher office.
- Documents connecting participants name will not be stored with collected study data.
- Data will be stored throughout the duration of the study and afterwards for data analysis.
- The researcher and other authorized individuals involved in the research study at Drexel University will see participant health information during and may give out health information during the research study. These include the researcher and the research staff, the institutional review board and their staff, legal counsel, research office and compliance staff, officers of the organization and other people who need to see the information in order to conduct the research study or make sure it is being done properly.
- Audio and video recordings will be taken during each 'Zoom' therapy session. Recordings will be kept on password encrypted usb drives and stored in a locked office only accessible to the principle investigator and adherence coder.
- Participant health information may be disclosed or transmitted electronically.

Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission.

Describe any procedures that will be used for quality control of collected data.

Data management efforts will be led by the PI. The study data will include all study assessment measures and signed consent forms. Data will be collected (identified only using the subjects' ID number) and managed electronically using REDCap. For data analysis purposes, the deidentified data will be downloaded onto the password protected computers of the investigators for analysis in SPSS. The PI will periodically review data for completeness, out of range data, etc.

Subjects' identifying information (name, address, etc.) is stored separately from other data collected in a locked file cabinet in a locked office and is only accessible by members of the research team. Data will be kept as

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computer data files (self-report questionnaire data, lung function data and BMI data; and clinic visit attendance data from the patient's electronic medical record and voice recordings for treatment fidelity ratings).

Computer data files (MP3 files of voice recordings) will be stored only on Dr. O'Hayer's computer, in a locked office. Audio and video recordings will be taken during each 'Zoom' therapy session. Recordings will be kept on password encrypted usb drives and stored in a locked office only accessible to the principle investigator and adherence coder.

Data will be stored for seven years after study completion, as per institutional policies and procedures

11) Provisions to Monitor the Data to Ensure the Safety of Subjects

This is required when research involves more than Minimal Risk to subjects, otherwise indicate as Not Applicable N/A.

The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.

Describe:

- *The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.*
- *What data are reviewed, including safety data, untoward events, and efficacy data.*
- *How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).*
- *The frequency of data collection, including when safety data collection starts.*
- *Who will review the data.*
- *The frequency or periodicity of review of cumulative data.*
- *The statistical tests for analyzing the safety data to determine whether harm is occurring.*
- *Any conditions that trigger an immediate suspension of the research.*

The current study is of minimal risk. Data will be monitored for any serious psychological issues that arise. We will remain cognizant of the possibility that this line of questioning may bring out difficult psychological issues. The Office of Regulatory Research Compliance will be contacted as soon as the research team becomes aware of an unforeseen or unanticipated risk. Patients' therapists will further assess patients' suicidality and, in consultation with their supervisor (Dr. O'Hayer), make recommendations (e.g., more intensive outpatient therapy; inpatient hospitalization) as appropriate. If a participant is experiencing suicidal thoughts, urges, or actions during their participation in the study they may contact Dr. O'Hayer directly at 919-943-6738.

12) Withdrawal of Subjects

Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent.

Describe any procedures for orderly termination.

Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.

Subjects will be free to withdraw from the study at any time. No further data will be collected on the subject once they have withdrawn from the study.

13) Risks to Subjects

List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to the subjects' participation in the research. Include as may be useful for the IRB's consideration, describe the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks.

If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.

If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.

If applicable, describe risks to others who are not subjects.

Risks:

The study questionnaires are routinely used in clinical care and research with individuals with CF, but there is a low probability that some patients may experience mild discomfort in answering some questions. In addition, there is a very low but possible risk of accidental disclosure of PHI. Also, some patients may be identified as being suicidal based on their responses on the Beck Depression Inventory.

Steps to reduce risks:

1) Participants will be reminded that participation is voluntary and that they can refrain from answering any question. Interviewers will be encouraged to be sensitive to signs of potential discomfort from participants in responding to questions. 2) PHI will be protected by using only identification numbers on all study questionnaires. All study data files will be kept in Drexel RedCap. 3) Patients' therapists will further assess patients' suicidality and, in consultation with their supervisor (Dr. O'Hayer), make recommendations (e.g., more intensive outpatient therapy; inpatient hospitalization) as appropriate. 4) If a participant is experiencing suicidal thoughts, urges, or actions during their participation in the study they may contact Dr. O'Hayer directly at 919-943-6738.

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If a risk happens:

The Office of Regulatory Research Compliance will be contacted as soon as the research team becomes aware of an unforeseen or unanticipated risk.

Benefits:

Participants may experience improvements in decreased anxiety and depressive symptoms, and increased adherence to their medical regimen

Risks vs benefits:

Anxiety, depression, and nonadherence to medical regimen are common problems among individuals with CF. If ACT is found to be effective, then it may be used with CF populations throughout society to enhance their emotional and physical well-being. Accordingly, the potential benefits outweigh the potential risks.

14) Potential Benefits to Subjects

Describe the potential benefits that individual subjects may experience from taking part in the research. Include as may be useful for the IRB's consideration, the probability, magnitude, and duration of the potential benefits.

Indicate if there is no direct benefit. Do not include benefits to society or others.

Subjects will potentially benefit from counseling sessions to help with anxiety and depression issues. We are hopeful that these counseling sessions will translate into improved medication compliance along with better lung health, fewer exacerbations, and better compliance with medical appointments.

15) Vulnerable Populations

If the research involves individuals who are vulnerable to coercion or undue influence, describe additional safeguards included to protect their rights and welfare.

- *If the research involves pregnant women, review "CHECKLIST: Research Involving Pregnant Women (HRP-412)" to ensure that you have provided sufficient information.*
- *If the research involves prisoners, review "CHECKLIST: Research Involving Prisoners (HRP-415)" to ensure that you have provided sufficient information.*
- *If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children"), review the "CHECKLIST: Research Involving Children (HRP-416)" to ensure that you have provided sufficient information.*

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- *If the research involves cognitively impaired adults, review “CHECKLIST: Research Involving Cognitively Impaired Adults (HRP-417)” to ensure that you have provided sufficient information.*

Not applicable. No vulnerable subjects will be included in this study.

16) Multi-Site Research

Sites associated with this research study include:

1. Children’s Hospital of Philadelphia
 2. University of Pennsylvania Medical Center
 3. Adult Cystic Fibrosis Center at Drexel Pulmonary Medicine
 4. St. Christopher’s Hospital for Children
 5. Duke University Medical Center
 6. Augusta University
 7. University of Pittsburgh
- Duke University Medical Center has IRB in progress.
 - Augusta University Medical Center and University of Pittsburgh have ceded IRB to Drexel.
 - All sites have the most current version of the protocol, consent document, and HIPAA authorization (when applicable).
 - All required approvals have been obtained at each site (including approval by the site’s IRB of record).
 - All modifications have been communicated to sites, and approved (including approval by the site’s IRB of record) before the modification is implemented.
 - All engaged participating sites will safeguard data as required by local information security policies.
 - All local site investigators conduct the study appropriately.
 - All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.

Describe the method for communicating to engaged participating sites:

Primary method for communication will be email for site-to-site, with a site initiation visit at the start of the study and monthly conference calls to check on study progress.

17) Community-Based Participatory Research

Describe involvement of the community in the design and conduct of the research.

Note: “Community-based Participatory Research” is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. Community-based Participatory Research begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Not applicable.

18) Sharing of Results with Subjects

Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject’s primary care physicians) and if so, describe how it will be shared

The results of questionnaires will be shared with each subject after data analysis is complete. This way subjects will get feedback about their responses, and see potential future areas of need for treatment and further counseling.

19) Setting

Describe the sites or locations where your research team will conduct the research.

Identify where your research team will identify and recruit potential subjects.

Research subjects will be recruited at 219 N Broad Street 9th floor, where the adult cystic fibrosis clinic takes place on Tuesday afternoons and Friday afternoons, or at their clinic site if not a Drexel subject. Co-pi Chelsi Nurse will travel to the offsite location to do the consenting in person. Chelsi Nurse will obtain consent at Children’s Hospital of Philadelphia, University of Pennsylvania Medical Center, Adult Cystic Fibrosis Center at Drexel Pulmonary Medicine, and St. Christopher’s Hospital for Children.. Referrals may be accepted from Cystic Fibrosis centers not participating in this study, and in this case Chelsi Nurse will travel to the local CF clinic and consent each of these subjects in person. Subjects will be recruited from remote sites (Duke Univ Med Center, Augusta Univ, U Pittsburg) by our on-site representatives Chris Drescher (Augusta University), Patrick Smith and current research assistants (Duke University) and the current Cystic Fibrosis social worker (University of Pittsburg). All inputting of data will take place in the pulmonary offices on the 8th floor of 1427 Vine Street, where the co-pi and research

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coordinator, Chelsi Nurse has a locked office and password protected computer. All data will be inputted into Drexel Redcap, and data analysis will take place within SPSS.

Recruitment Sites:

- Children's Hospital of Philadelphia
- University of Pennsylvania Medical Center
- Adult Cystic Fibrosis Center at Drexel Pulmonary Medicine
- St. Christopher's Hospital for Children
- Duke University Medical Center
- Augusta University
- University of Pittsburg

Identify where research procedures will be performed.

Where will research be performed:

Therapy sessions will be administered via "Zoom" video conferencing system.

- *Describe the composition and involvement of any community advisory board.*

Not Applicable.

- *For research conducted outside of the organization and its affiliates describe:*

Site-specific regulations or customs affecting the research for research outside the organization.

Local scientific and ethical review structure outside the organization.

Not Applicable.

20) Resources Available

Describe the resources available to conduct the research: For example, as appropriate:

- *Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?*
- *Describe the time that you will devote to conducting and completing the research.*

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- *Describe the number and qualifications of your staff by describing their experience in conducting research, their knowledge of the local study sites, culture, and society.*
- *Describe your facilities.*
- *Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research.*
- *Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.*

Sample size determination: 105 participants in each treatment condition (ACT vs TAU) to be recruited over 3 years will allow us to detect a medium group difference (medium effect size) with 95% confidence ($p < .05$).

Treatment Fidelity

All therapy providers will undergo training in our ACT with CF manualized protocol, and our supportive psychotherapy (treatment as usual) protocol. Clinicians will meet with Dr. O'Hayer weekly for clinical supervision.

Participants in both the ACT with CF and TAU groups will complete primary endpoint and secondary endpoint measures at baseline, six weeks, and three months after study initiation.

Data will be stored for seven years after study completion, as per institutional policies and procedures.

To ensure treatment fidelity, a trained coder will watch the videotaped recording of a random sample of ACT with CF sessions and a random sample of treatment as usual sessions, coding each for adherence to the ACT with CF manual (in the case of the ACT condition), and absence of ACT-based interventions (in the case of the treatment as usual condition).

At this time, we have just over 100 patients in our Drexel Adult cystic fibrosis clinic.

Given the levels of anxiety and depression in our clinic, we believe we will be successful recruiting fifty patients out of 100 total. We also anticipate recruiting subjects from other CF sites, and target a total of 210 subjects altogether. During every clinic visit, patients will be screened for potential involvement in the study. Cystic fibrosis patients typically attend an outpatient visit four times per year.

21) Prior Approvals

Describe any approvals that will be obtained prior to commencing the research. (E.g., school, external site, funding agency, etc.)

Not applicable.

22) Recruitment Methods

*Describe when, where, and how potential subjects will be recruited.
Describe the source of subjects.*

Potential subjects will be recruited at the following sites:

- Children's Hospital of Philadelphia
- University of Pennsylvania Medical Center
- Adult Cystic Fibrosis Center at Drexel Pulmonary Medicine
- St. Christopher's Hospital for Children
- Duke University Medical Center
- Augusta University
- University of Pittsburg

Describe the methods that will be used to identify potential subjects.

Main Inclusion Criteria

- Men and women aged 18 and above.
- Able to read/understand English.
- Diagnosis of cystic fibrosis.
- PHQ-9 score > 4 or GAD-7 score > 4.

Describe materials that will be used to recruit subjects. (Attach copies of these documents with the application. For advertisements, attach the final copy of printed advertisements. When advertisements are taped for broadcast, attach the final audio/video tape. You may submit the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.)

Not Applicable.

23) Number of Subjects

Indicate the total number of subjects to be accrued locally.

If applicable, distinguish between the number of subjects who are expected to be enrolled and screened, and the number of subjects needed to complete the research procedures (i.e., numbers of subjects excluding screen failures.)

Sample size determination: 105 participants in each treatment condition (ACT vs TAU) will allow us to detect a medium group difference (medium effect size) with 95% confidence ($p < .05$).

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IF THIS PROTOCOL INVOLVES ACCESS AND REVIEW OF MEDICAL OR ELECTRONIC RECORDS INDICATE THE MAXIMUM NUMBER OF RECORDS YOU INTEND TO REVIEW.

Data will be obtained for all 210 subjects.

24) Confidentiality

If this is a multicenter study, describe the local procedures for maintenance of confidentiality.

- *Where and how data or specimens will be stored locally?*
- *How long the data or specimens will be stored locally?*
- *Who will have access to the data or specimens locally?*
- *Who is responsible for receipt or transmission of the data or specimens locally?*
- *How data and specimens will be transported locally?*

The researcher and other authorized individuals involved in the research study at Drexel University will see participant health information during and may give out participant health information during the research study. These include the researcher and the research staff, the institutional review board and their staff, legal counsel, research office and compliance staff, officers of the organization and other people who need to see the information in order to conduct the research study or make sure it is being done properly. Participant health information may be disclosed or transmitted electronically. Audio and video recordings will be taken during each 'Zoom' therapy session. Recordings will be kept on password encrypted USB drives and stored in a locked office only accessible to the principle investigator and adherence coder.

Other persons and organizations outside of Drexel University may see and use participant health information during this research study.

Governmental entities that have the right to see or review participant health information, such as The Office for Human Research Protections.

Doctors and staff at the hospital where this research study will take place.

If participant health information is given to someone not required by law to keep it confidential, then that information may no longer be protected, and may be used or given out without participant permission.

25) Provisions to Protect the Privacy Interests of Subjects

Describe the steps that will be taken to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact or whom they provide personal information.

Describe what steps you will take to make the subjects feel at ease with the research situation in terms of the questions being asked and the

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procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures.

Indicate how the research team is permitted to access any sources of information about the subjects.

Participant health information will be used and given out to carry out the research study and to evaluate the results of the study.

Participant information may also be used to meet the reporting requirements of governmental agencies.

Participants do not have to give your authorization to use or give out health information. However, if participants do not give authorization, you cannot participate in this research study.

At any time participants may cancel authorization to allow health information to be used or given out by sending a written notice to Human Research Protection at 1505 Race Street, 7th Floor Bellet Bldg, Philadelphia, Pennsylvania, 19102. If participants leave this research study, no new health information will be gathered. However, information gathered before that date may be used or given out if it is needed for the research study or any follow-up.

Participant authorization to use and give out health information will continue until they withdraw or cancel their authorization. After the research study is finished, their health information will be maintained in a research database. Drexel University shall not re-use or re-disclose the health information in this database for other purposes unless you give written authorization to do so. However, the Drexel University Institutional Review Board may permit other researchers to see and use participant health information under adequate privacy safeguards.

Participants have the right to look at their medical records at any time during this research study. However, the researcher does not have to release research information to participants if it is not part of their medical record.

26) Economic Burden to Subjects

Describe any costs that subjects may be responsible for because of participation in the research.

Not applicable

27) Consent Process

Indicate whether you will you be obtaining consent, and if so describe:

- *Where will the consent process take place?*
- *Any waiting period available between informing the prospective subject and obtaining the consent. (In general subjects should not be rushed or felt "pressured" to consent to research)*
- *Any process to ensure ongoing consent.*

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- *Whether you will be following “SOP: Informed Consent Process for Research (HRP-090).” If not, describe:*

The role of the individuals listed in the application as being involved in the consent process.

The time that will be devoted to the consent discussion.

Steps that will be taken to minimize the possibility of coercion or undue influence.

Steps that will be taken to ensure the subjects’ understanding.

We will be following “SOP: Informed Consent Process for Research (HRP-090)” procedures. Consent will take place at each recruitment site’s Cystic Fibrosis Clinic. There is no planned waiting period between informing potential subjects of the study and obtaining consent, although patients can certainly defer enrolling in the study if they would like to consult with their physician, lawyer, family members, etc.

Non-English Speaking Subjects

Not applicable

Subjects who are not yet adults (infants, children, teenagers)

- *Describe the criteria that will be used to determine whether a prospective subject has not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted. (E.g., individuals under the age of 18 years.)*

For research conducted in the state, review “SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)” to be aware of which individuals in the state meet the definition of “children.”

For research conducted outside of the state, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have legal counsel or authority review your protocol along the definition of “children” in “SOP HRP 013: Legally Authorized Representatives, and SOP HRP 014: Children, and Guardians.”

- *Describe whether parental permission will be obtained from:*

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Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

- *Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission.*
- *Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent.*
- *When assent of children is obtained describe whether and how it will be documented.*

Not applicable.

Cognitively impaired adults

Not applicable.

Adults Unable to Consent

Not applicable.

28) Process to Document Consent in Writing

Describe whether you will be following “SOP: Written Documentation of Consent (HRP-091).” If not, describe whether and how consent of the subject will be documented in writing.

If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent.

(If you will document consent in writing, attach a consent document. If you will obtain consent, but not document consent in writing, attach a consent script. Review “CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)” to ensure that you have provided sufficient information. You may use “TEMPLATE CONSENT DOCUMENT (HRP-502)” to create the consent document or script.)

Study personnel will be following “SOP: Written Documentation of Consent (HRP-091)”. The study consent form is attached.

29) Drugs or Devices

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*If the research involves drugs or device, describe your plans to store, handle, and
administer those drugs or devices so that they will be used only on subjects and
be used only by authorized investigator*

Not applicable (Although subjects will be taking medication as part of their
clinical care, the study itself is examining questions related to adherence, both to
medications and to counseling).